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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,355	04/10/2001	Imre Kovesdi	205654	9085

23460 7590 04/25/2003

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	15

DATE MAILED:

This is a communication from the examiner in charge of your application.
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OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 3/4/03

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s); or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-9, 12, 13, 16-19, 20-28, 30-41, 43-46 is/are pending in the application.
Of the above, claim(s) 8, 13, 20-28, is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-7, 9, 12, 16-19, 30-41, 43-46 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-9, 12, 13, 16-28, 30-41, 43-46 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9, 12
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

* U.S. GPO: 1996-404-496/40517

Part III: Detailed Office Action

Copies of the information disclosures submitted 9/24/01 (paper number 9) and 8/5/02 (paper number 12) are enclosed.

In response to the rejection under 35 U.S.C. § 112, second paragraph on the basis that the claims are unclear because it is not clear to *which* flk or flt receptors the VEGF-A portion of the polypeptide binds with a lower affinity than to KDR receptors, applicants have argued that they intend any and all flk or flt receptors. As pointed out in the previous Office Action at page 3, not all flk or flt receptors bind VEGF-A *at all*, specifically it is known in the art that VEGF does not bind to flk-2 receptors. Accordingly, while not indefinite, it is noted that *any* VEGF-A that binds to a KDR receptor with *any* affinity would meet the limitations of claim 2.

With respect to the rejection of Claim 17 under 35 U.S.C. § 112, second paragraph, Applicants traversal that the term is commonly used in the art, is noted. The Examiner notes that the page of Stedman's medical dictionary referenced at page 6 of paper number 15, submitted 3/4/03, was not attached to the response. However, 'dilatation', as defined by Webster's online dictionary (**www.m-w.com**) is the condition of being stretched beyond normal dimensions especially as a result of overwork, disease, or abnormal relaxation. Accordingly, the Examiner will interpret that portion of claim 17 as indicating that the second peptide portion comprises a peptide which cause blood vessel walls to be stretched beyond their normal dimensions.

Accordingly, all grounds of rejection under 35 U.S.C. § 112, second paragraph have been overcome by Applicants amendments or arguments.

Applicants amendments to the claims to recite that the second peptide lacks a collagen binding domain overcomes the rejection of claims 1-5, 9, 17, 18, 32-36, and 39-41 under 35 U.S.C. 102(e) as being anticipated by Hall et al., U.S. Patent Number 6,387,663.

Objections and Rejections under 35 U.S.C. §112:

New Matter:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 31 has been amended to recite that the fusion protein comprises an N-terminal truncated form of HBNF or MK including "at least about 60% of the wild-type HBNF or MK amino acid sequence. Applicants point to paragraph [0063] for support for this limitation. However, examination of that paragraph reveals only disclosure of "about 70% *or less*, more preferably about 65% or less, and even more preferably about 60% or less...". There is no disclosure of the now-claimed "at least about 60%", which is equivalent to '60% or *more*', which would include species with greater than 70%, the highest number recited.

Enablement:

Claims 1-7, 9, 12, 16-19, 30-41, and 43-46 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention in a manner commensurate in scope with the claims.

It is noted that applicants have amended the claims to indicate that the first portion of the fusion protein has at least 80% homology to VEGF-A, thus reducing issues under 35 U.S.C. § 112,

first paragraph. However, several issues remain:

1) Claims 1 and 43 (for example) recite that the VEGF portion may have bone growth promoting activity; such is not an art-recognized property of VEGF, and is neither described or enabled by the specification as originally filed. While Carlevaro et al., cited by applicants , teach that VEGF is *associated* with neovascularization in cartilage, such is not equivalent to bone growth. Further, the finding that chondrocytes express VEGF is also not indicative of bone growth induction *by* VEGF. Bone growth is a complex process. While neovascularization is required for bone growth, and VEGF may be required for such neovascularization, presence of VEGF alone has not been shown to be a causative factor in induction of bone growth. Accordingly, the specification is not enabling of this property as applied to VEGF. Applicants traversal of this ground of rejection has been fully considered but is not deemed persuasive. Applicants cite a paper by Ferrara as showing that VEGF-dependent blood vessels are essential for coupling apoptosis of hypertrophic chondrocytes with bone formation. It is noted that the paper by Ferrara has not properly been made of record in an information disclosure statement, and has been considered only to the extent to which it is cited in applicants traversal. However, the Examiner finds that the citation of Ferrara is consistent with the original rejection. Ferrara supports the Examiner's original conclusion, restated above, that "While neovascularization is required for bone growth, and VEGF may be required for such neovascularization, presence of VEGF alone has not been shown to be a causative factor in induction of bone growth". Merely because VEGF is necessary for proper blood vessel formation which formation is required for bone growth, does not mean that VEGF itself in any way *promotes* bone growth. In fact, there are numerous sites in the body that have VEGF-induced vessel formation, and at which bone growth not only does not occur, but would be undesirable. Further, Ferrara, at the paragraph cited by applicants, even states that "the *vasculature* carries the essential cellular and humoral signals required for correct growth plate morphogenesis" (emphasis added). Accordingly, Ferrara supports the Examiner's position that while VEGF is required for vessel formation, which vessel formation is necessary for bone growth, VEGF itself does not in any way promote bone growth. It remains that this is a property of VEGF not known in the art, and not

enabled by the specification as originally filed.

2) The specification does not provide adequate written description or enablement of the scope of claimed "second non-VEGF peptide portion" with angiogenesis or bone growth promoting activity. This rejection is maintained for reasons set forth at pages 7-8 of the previous Office Action. Applicants traversal at pages 8-9 of paper number 15 has been fully considered but is not deemed persuasive. As applicants state in their argument, "Satisfactory disclosure of a "representative number" depends on whether one of ordinary skill in the art would recognized that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. It remains that, as stated in the original rejection, the specification has defined such in a manner that is so broad that any possible functional equivalent is encompassed. While there are numerous possible cytokines disclosed that could be the 'second' portion, the definitions in the specification encompass all possible derivatives of such, see for example paragraphs 0050-0051. As all functional equivalents of all possible proteins with the stated activity are encompassed, clearly the written description in the specification as originally filed does not support such, for reasons analogous to those above, and clearly enablement is not commensurate with such scope. With further respect to enablement, the Examiner notes the statement that the purpose of the invention is that "there remains a need for therapeutic fusion proteins which exhibit improved therapeutic potential over those presently known in the art". While the Examiner takes no issue with that statement, that is not a license for applicants to disclose and claim all possible such fusion proteins without any disclosure of the particular properties of the fusion proteins, and hence how such would be used. The claims, which encompass innumerable possible species, are merely an invitation to stick two proteins together and then discover what particular properties the combination has, and hence develop uses for such. Such an invitation to experiment is not enabling. The fact that the specification discloses how to make vectors and express recombinant proteins is not pertinent to this ground of rejection; the issue here is that there is insufficient written description and enablement of a commensurate number of species of the protein to be so expressed. Without

knowing what the protein is, one cannot make it, regardless of the now-routine nature of recombinant DNA technology.

3) It remains that there is no written description or enablement of fusion proteins with a half life at least twice as long as either the first or second peptide portion or both as claimed in claim 6, or of at least 10 minutes, as in claim 7. This is merely a desired property. The specification as filed does not disclose the half-lives of the various proteins, nor does it provide any data or working example of the half-life of any of the claimed fusion proteins. Half-life is a property of a protein, as well as of the biological system with which that protein is interacting. It is not recognized in the art that half-life is a predictable property. Hence, given the breadth of the claims, the lack of predictability in the art, the lack of guidance and absence of working examples, the specification is not enabling of proteins with the recited half-lives.

Applicants traversal at page 9 of paper number 15 has been fully considered but is not deemed persuasive. Applicants argue that the disclosure at paragraph [00108] provides sufficient disclosure, and that the prior art demonstrates that the person of ordinary skill in the art knows how to determine half-lives of proteins. This argument has been fully considered but is not deemed persuasive because it fails to address the ground of rejection, namely that the specification as filed does not disclose the half-lives of the various proteins, nor does it provide any data or working example of the half-life of any of the claimed fusion proteins. The specification provides only a wish, and no guidance as to how that wish is to be achieved. As stated in the original rejection, the art of increasing half-lives of proteins is not predictable, and the specification has provided no specific guidance nor working examples as to how to achieve the 'goals' in the claims. Accordingly, the rejection is maintained.

4) It remains that there is inadequate written description and enablement to support the scope of fusion proteins that result in vessels that are associated with more smooth muscle cells, a greater concentration of smooth muscle cells, more endothelial cells, a greater concentration thereof, or a

combination of such than would be obtained using only the 'VEGF' portion of the protein (claim 12), both generically and with respect to the elected species of second peptide, HBNF. Once again, the claim is merely stating a desired property of the claimed protein, and the specification does not provide guidance as to what types of proteins provide such properties, or how one would modify a protein to do so. Merely disclosing a few proteins that might have one of the claimed properties is insufficient to describe or enable the scope of the claims which encompass any and all proteins having said properties, for reasons cited above. With particular respect to the elected species, HBNF, none of those properties have been recognized as being associated with HBNF in the art, and the specification provides no guidance or working examples of HBNF with such properties. As stated above, the art of protein engineering is unpredictable, and it would not be expected that HBNF could be engineered to have such properties without undue experimentation. Accordingly, such is not enabled for the elected species. Applicants traversal bridging pages 9-10 of the response to the effect that "a representative number of species" has been disclosed and that methods of measuring the desired goals are known in the art has been fully considered but is not deemed persuasive. While applicants aver that a representative number of species meeting the limitations of claim 12 have been disclosed, they fail to point out even a single such species in the argument. Accordingly, the Examiner maintains that the disclosure is not commensurate in scope with the claims. With respect to the elected species, applicants argue at page 10 of the response that papers by Souttou et al. and Papadimitriou et al. support the assertions of activity found in claim 12 as drawn to HBNF. No article by Souttou et al. accompanied applicants response, so such cannot be evaluated. With respect to the Papadimitriou article, it is noted that Papadimitriou's article was published after the filing date of the instant invention, and therefore cannot be relied upon to establish the state of the art at the time the invention was made. The article was cited by the Examiner in making the original rejection, as evidence of unpredictability; while unpredictability can be shown after the filing date, post-filing date references are *not* effective to demonstrate what was known at the time the invention was made. Further, Papadimitriou's disclosure that HBNF is an endothelial cell mitogen would not be sufficient to enable an assertion that blood vessels resulting from the administration of the

claimed fusion protein, wherein said fusion protein comprises HBNF, would have "more smooth muscle cells, a greater concentration of smooth muscle cells, more endothelial cells, a greater concentration of endothelial cells, or any combination thereof, than blood vessels resulting from administration of a protein consisting essentially of the first peptide portion", as in claim 12. While HBNF would be expected to act as an endothelial cell mitogen, it is not predictable that such activity would alter the nature of the fully-developed blood vessels that might result from the administration of the claimed fusion protein. While Papadimitriou reports that HBNF stimulates angiogenesis in a chicken model system, there is no report of the vessels so formed differing in any way from any other vessels. Accordingly, Papadimitriou (a) cannot be cited to establish the state of the art, and (b) even if it could, would not support the assertions in claim 12.

5) It remains that there is inadequate written description and enablement to support claims to proteins having the properties recited in claim 17, both generically and with respect to the elected species. Claim 17 lists a number of additional properties of the second peptide. In addition to the lack of written description and enablement of the second peptide itself for reasons above, there is no written description or guidance as to how such is to be achieved, and no working examples. Accordingly, the examiner concludes that the specification does not describe or enable these properties. Although they may be possessed by one or more species, the specification has not provided guidance as to which species, or how to make such. With respect to the particularly elected species, HBNF, once again, none of these properties have been reported for HBNF, the specification has neither described species of HBNF with those properties, nor has it enabled how to make or use such.

Applicants argue at pages 10-11 of the response that the specification at paragraph [0048] discloses a commensurate number of species to enable claim 17. This argument has been fully considered but is not deemed persuasive because paragraph [0048] merely provides one or two examples of cytokines or cytokine families that are asserted to have the claimed properties, and seeks to claim any fusion protein comprising any protein with such properties. Further, with respect to

HBNF in particular, applicants assert that HBNF has been shown to promote angiogenesis by promoting endothelial cell proliferation, migration, survival, and capillary-like structure formation. These are not the properties claimed in claim 17. Merely because endothelial cell migration and formation of capillary-like tubes requires degradation of extracellular matrix, does not equate to a showing that HBNF itself degrades extracellular matrix. Papadimitriou, even if it were available as a reference to demonstrate the state of the art at the time the invention was made, makes no such conclusion.

6) The specification has not taught how to use proteins comprising VEGF and HBNF. Papadimetriou et al., cited by applicants, disclose that soluble HBNF had *no* effect on the proliferation of bovine brain capillary cells, HUVEC, or rat adrenal medulla microvascular endothelial cells. Therefore, it is not predictable that a soluble fusion protein comprising HBNF would be able to do otherwise. Imai et al., also cited by applicants, disclose that HBNF "is expressed by osteoblasts/osteoplast precursors", is extracellular matrix-associated, and binds syndecan. Imai et al. also reported that soluble HBNF inhibited osteoblast recruitment in a dose dependent manner (see Fig. 3). Thus, one of ordinary skill in the art would not expect a soluble protein comprising HBNF to *promote* bone growth. With respect to angiogenic activity, Choudhuri et al., cited by applicants, report angiogenic activity of HBNF on breast carcinoma cells. However, this is not predictive of angiogenic activity on other cells, and would not be predictive of how to use HBNF to stimulate angiogenesis. This conclusion is supported by Relf et al., cited by applicants, who state that "Angiogenesis in tumors, However, is quite different from that seen in normal tissues, with leaky vessels, aberrant blood flow, and areas of necrosis, as well as increased vascularity." Hence, although HBNF may have angiogenesis-related activity in mammary tumors, the art does not recognize it as an angiogenic factor, and neither the art nor the specification as filed have taught how to use it for such; what types of cells, and under what conditions. Further, HBNF in a breast carcinoma and the test systems used by Choudhuri et al. was in membrane bound form, and not soluble, as it would be in the claimed fusion protein. As taught by Papadimetriou and discussed

above, the activity of membrane-bound HBNF is not predictive of the activity of soluble HBNF. Finally, there are no reports in the art of any role for HBNF in wound healing, as in claim 30. Applicants traversal at page 11 of the response has been fully considered but is not deemed persuasive. Applicants argue that Imai and Papadimitriou actually support the asserted uses. This argument has been fully considered but is not deemed persuasive because as stated in the rejection above, both references teach that soluble forms of the protein act very differently from bound forms of the protein, and that when the protein was in soluble form, the activities claimed by applicants were not observed. As the specification is silent with respect to *how* to use the claimed proteins to achieve the desired effects, the Examiner maintains that the specification as originally filed fails to enable the claimed properties for the claimed proteins.

Thus, it remains that at the time the specification was filed, the only predictable activities of the claimed soluble protein comprising VEGF and HBNF would have been angiogenic activity due to the VEGF, neurite outgrowth activity due to the HBNF, and the ability to inhibit osteoblast recruitment, due to the soluble HBNF. The specification as originally filed has not taught how to use a protein with those properties; it is not clear for what conditions or methods of treatment such a protein would be desirable. Accordingly, the specification as originally filed fails to teach how to use the elected species.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

> section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-4, 9, 16-19, 32-34, 39-40, and 43-45 are rejected under 35 U.S.C. 102(a) as being anticipated by Davis et al., WO 00/37642, cited by applicants. This rejection is maintained for reasons of record. Applicants arguments have been fully considered but are not deemed persuasive. Applicants argue that angiopoietin does not separately promote angiogenesis or bone growth. This argument has been fully considered but is not deemed persuasive because Thurston et al., cited as evidence in the rejection, clearly states that VEGF and angiopoietin-1 function together during vascular development, with VEGF acting during early vessel formation, and angiopoietin-1 acting later during vessel remodeling, maturation and stabilization (see abstract). Thus, *separate* from VEGF-1, in the sense that they do not act together to cause the same effect, Ang-1 clearly promotes angiogenesis, at a later stage in the process than VEGF. The Examiner further notes that Ang-1 is specifically disclosed as a species of 2nd peptide, at paragraph [0050] of the specification, and that the claims do not, contrary to applicants arguments, require a multimerizing domain.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and

invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 9, 17, 18, 32-34, 41, and 43-46 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yoon et al., Life Sciences 64(16):1435-1445, 1997, cited by applicants, in view of either or both of Gill et al., U.S. Patent Number 6,291,667 and Rockwell et al., U.S. Patent Number 5,874,542 for reasons of record. Applicants argue that the prior art teaches away from the invention, as VEGF is known to promote tumor angiogenesis. This argument has been fully considered but is not deemed persuasive because it is well known in the art to use receptors to target cytotoxic agents to tumors. Although VEGF would, alone, be contraindicated for administration to a tumor, as a fusion protein with angiogenin, it would be expected to be cytotoxic as set forth in the rejection, and thus *not* to cause angiogenesis and further tumor growth. Applicants argument is further belied by the fact that the same argument could be made for the protein of Yoon et al., the primary reference, with respect to EGF; clearly, applicants scenario of stimulating tumor growth was not a problem for Yoon et al.

Accordingly, the invention, taken as a whole, is *prima facie* obvious over the cited prior art.

Advisory Information:

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the

date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, However, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

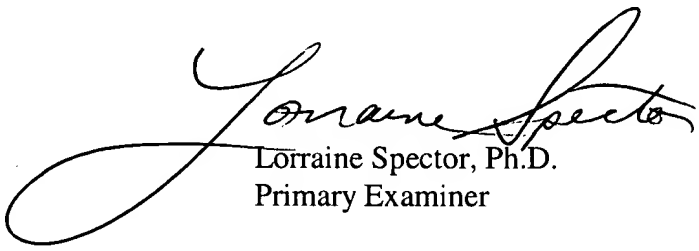
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.



Lorraine Spector, Ph.D.
Primary Examiner

09/832355.2
4/24/03